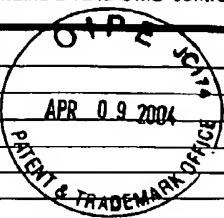


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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	10/618,835
Date Submitted: April 9, 2004 <i>(use as many sheets as necessary)</i>				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	1	of	1	Attorney Docket Number	080618-0237



U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code <sup>2</sup> (if known)		
DRL	D1	5,372,807		POIANI et al.	12-13-1994
DRL	D2	5,278,189		RATH et al.	01-11-1994

Class / Subclass

Pages, Columns, Lines,  
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Passages or Relevant  
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424 / 78,36  
514 / 561

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)	
DRL	D3	WO	88/01872	Dudrick Medical Research	03-24-1988
DRL	D4	EP	0 483 614 A	NB Int'l. Technologies	05-06-1992
DRL	D5	WO	94/16729 A	Neorx Corporation	08-04-1994
DRL	D6	GB	953,997	AEC Chim. Organ. Biolog.	04-02-1964
DRL	D7	EP	0 546 796 A1	Ajinomoto Co., Inc.	06-16-1993
DRL	D8	WO	94/28721 A	Univ. Leland Stanford Jr.	12-22-1994
DRL	D9	GB	1,304,499	Tixier, Madeleine	01-24-1973

Class / Subclass

Pages, Columns, Lines,  
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T<sup>6</sup>

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			
DRL	D10	RIBEIRO, ALDA, et al., "Arginine-Lysine Combination in Immunodepressed Elderly Patients, Long-Term Controlled Trial," <i>Clinical Trials Journal</i> 1986, United Kingdom, vol. 23, no. 3, pp. 185-192.			
DRL	D11	IGNARRO, LOUIS J., et al., "Basic Polyamino Acids Rich in Arginine, Lysine, or Ornithine Cause Both Enhancement of and Refractoriness to Formation of Endothelium-Derived Nitric Oxide in Pulmonary Artery and Vein," <i>Circulation Research</i> , vol. 64, no. 2, 1989, pages 315-329.			

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Examiner Signature	Jeffrey E. Russel	Date Considered	September 8, 2004
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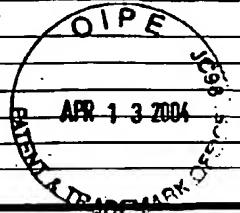
(use as many sheets as necessary)

Sheet 1 of 1

**Complete if Known**

<b>Application Number</b>	10/618,835
<b>Filing Date</b>	07/15/2003
<b>First Named Inventor</b>	John P. Cooke
<b>Group Art Unit</b>	1654
<b>Examiner Name</b>	J. Russel

Attorney Docket Number 080618-0237

**U.S. PATENT DOCUMENTS**

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

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	E1	COOKE, JOHN P., et al., "Antiatherogenic Effects of L-Arginine in the Hypercholesterolemic Rabbit," <i>Journal of Clinical Investigation</i> , vol. 90, September 1992, pp. 1168-1172.	
	E2	MARIN, JESUS, et al., "Role of Endothelium-Formed Nitric Oxide on Vascular Responses," <i>General Pharmacology</i> , vol. 21, no. 5, 1990, pp. 575-587.	
	E3	JANSSENS, STEFAN P., et al., "Cloning and Expression of a cDNA Encoding Human Endothelium-derived Relaxing Factor/Nitric Oxide Synthase," <i>Journal of Biological Chemistry</i> , vol. 267, no. 21, July 25, 1992, pp. 14519-14522.	

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Jeffrey B. Russel

Date Considered

September 8, 2004

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Date Submitted: April 19, 2004

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Sheet	1	of	13	Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

## U.S. PATENT DOCUMENTS

Class 1 Subcl-55

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		Number	Kind Code <sup>2</sup> (if known)			
JPL	A1	2,878,124		KRUKENBERG	03-17-1959	514/557
JPL	A2	3,015,567		HAUSE et al.	01-02-1962	426/650
JPL	A3	3,360,374		BARR, SR. et al.	12-26-1967	726/615
JPL	A4	3,970,750		BROCKEMEYER et al.	07-20-1976	424/679
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JPL	A13	5,036,052		OZEKI et al.	07-30-1991	514/19
JPL	A14	5,041,429		SAWAI et al.	08-20-1991	514/193
JPL	A15	5,106,836		CLEMENS et al.	04-21-1992	514/21
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JPL	A21	5,262,435		JOSHUA et al.	11-16-1993	514/452
JPL	A22	5,278,189		RATH et al.	01-11-1994	514/561
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JPL	A34	5,576,287		ZALOGA et al.	11-19-1996	514/12
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JPL	A37	5,631,031		MEADE	05-20-1997	426/2
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JPL	A41	5,830,848		HARRISON et al.	11-03-1998	514/2
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JPL	A43	5,965,529		GARFIELD et al.	10-12-1999	514/12

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Examiner Signature	Jeffrey E. Russel	Date Considered	September 7, 2004
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Sheet	2	of	13	Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237

U.S. PATENT DOCUMENTS					Class / Subclass
<i>JPL</i>	A44	5,945,452		COOKE et al.	08-31-1999
<i>JPL</i>	A45	6,063,432		MAXWELL et al.	05-16-2000
<i>JPL</i>	A46	6,083,515		GARVEY et al.	07-04-2000
<i>JPL</i>	A47	5,348,755		ROY	09-20-1994
<i>JPL</i>	B1	5,229,390		MORIYAMA et al.	07-20-1993
<i>JPL</i>	B2	5,352,695		N'GUYEN et al.	10-04-1994

FOREIGN PATENT DOCUMENTS						Class / Subclass	
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
<i>JPL</i>	A48	JP	50-48189		04-30-1975		
<i>JPL</i>	A49	JP	57-5692		01-12-1982		
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<i>JPL</i>	A51	JP	58-55418		04-01-1983		
<i>JPL</i>	A52	EP	0441119A2	LEVERE et al.	08-14-1991		
<i>JPL</i>	A53	JP	3-21786		01-30-1991		
<i>JPL</i>	A54	EP	0511587	MORIYAMA	11-04-1992		
<i>JPL</i>	A55	EP	0511118A1	L'OREAL	10-28-1992		
<i>JPL</i>	A56	EP	0546796A1	SONAKA	06-16-1992		
<i>JPL</i>	A57	ZA	93-6619	DAVIS et al.	09-15-1993		
<i>JPL</i>	A58	WO	93-18156	BLOCH et al.	09-16-1993		
<i>JPL</i>	A59	JP	7-163269		06-27-1995		
<i>JPL</i>	A60	FR	2,547,501	DONZEAU	12-1984		

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<i>JPL</i>	A61	MERIMEE et al.; "Arginine infusion in maturity-onset diabetes mellitus"; <i>The Lancet</i> (June 11, 1966), pp. 1300-01.					
<i>JPL</i>	A62	DI ROSA, "Azione antiammoniemica ed epatoprotettiva di una associazione a base di piridolidonecarbossilato di ergosina, taurina e vitamina B <sub>6</sub> "; <i>Lavori ricevuti</i> (July 14, 1967).					
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<i>JPL</i>	A64	KADIRVEL et al.; "Uptake of L-Arginine and L-Lysine by the small intestine and its influence on Arginine-Lysine antagonism in chicks"; <i>Journal of Nutrition</i> , Vol. 103, No. 3 (March, 1974), pp. 339-43.					

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Examiner Signature	<i>Jeffrey E. Russel</i>	Date Considered	<i>September 7, 2004</i>
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Date Submitted: April 19, 2004

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Sheet

3

of

13

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Application Number	10/618,835
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First Named Inventor	John P. Cooke
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JR	A65	BARNES et al.; "The effect of calcium ions on the hydrolysis of benzylarginine ethyl ester by porcine enteropeptidase"; <i>Biochimica et Biophysica Acta</i> ; 452 (1976), pp. 161-64.	
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JR	A72	BARBUL et al.; "Arginine stimulates lymphocyte immune response in healthy human beings"; <i>Surgery</i> (08-1981) 90(2):244-51.	
JR	A73	BERSON et al.; "A Two Year Trial of Low Protein, Low Arginine Diets or Vitamin B <sub>6</sub> for Patients with Gyrate Atrophy"; <i>Birth Defects: Original Article Series</i> , Vol. 18, No. 6, pp. 209-218 (1982).	
JR	A74	KATAN et al.; "Reduction of Casein-induced Hypercholesterolemia and Atherosclerosis in Rabbits and Rats by Dietary Glycine, Arginine and Alanine"; <i>Elsevier North Holland Scientific Publishers, Ltd.</i> (1982). <i>Atherosclerosis</i> 43:381-91.	
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JR	A77	WALLER et al.; "Conditions for the synthesis of antioxidative arginine-xylose maillard reaction products"; <i>Synthesis of Antioxidative Products</i> (1983), pp. 125-40.	
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JR	A81	OLSON et al.; "Avian shell gland contractility: interaction of PGF <sub>2α</sub> and arginine vasotocin with Ca <sup>2+</sup> "; <i>American Journal of Physiology</i> Vol. 244, No. 3 (03-83), pp. C150-57.	

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Examiner Signature

Jeffrey E. Russel

Date Considered

September 7, 2004

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**OTHER - NON PATENT LITERATURE DOCUMENTS**

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XPL	A82	HERCHUELZ et al.; "Mechanism of arginine-stimulated Ca <sup>2+</sup> influx into pancreatic B cell"; <i>American Journal of Physiology</i> , Vol. 246, No. 1 (01-84), pp. E38-43.	
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XPL	A86	PALMER et al.; "Vascular endothelial cells synthesize nitric oxide from L-Arginine"; <i>Nature</i> (06-16-1984) 333:664-66.	
XPL	A87	BARBUL et al.; "Intravenous Hyperalimentation with High Arginine Levels Improves Wound Healing and Immune Function"; <i>Journal of Surgical Research</i> (04-1985) 63B:328-34.	
XPL	A88	HOSANG; "Suramin Binds to Platelet-Derived Growth Factor and Inhibits Its Biological Activity"; <i>Journal of Cellular Chemistry</i> (04-30-1985) 29:265-73.	
XPL	A89	WATANABE et al.; "Effects of Vitamin E and Arginine on the Metabolism of Alcohol"; <i>Nutrition Reports International</i> , Vol. 32, No. 1 (07-85), pp. 149-53	
XPL	A90	BARBUL; "Arginine: Biochemistry, Physiology, and Therapeutic Implications"; <i>Journal of Parenteral and Enteral Nutrition</i> (1986) 10(2):227-38.	
XPL	A91	VISEK; "Arginine Needs, Physiological State and Usual Diets. A Reevaluation"; <i>J. of Nutrition</i> (1986) 116:36-46.	
XPL	A92	ROSS; "The Pathogenesis of Atherosclerosis - An Update"; <i>The New England Journal of Medicine</i> , Vol. 311, No. 8 (02-20-86), pp. 488-500.	
XPL	A93	TAKAHARA et al.; "Calcium-dependent Properties of Peptidylarginine Deiminase from Rabbit Skeletal Muscle"; <i>Agric. Biol. Chem.</i> , 50 (11) (06-25-86), pp. 2899-2904.	
XPL	A94	JANSSENS et al.; "Calcium-independent stimulation of glycogenolysis by arginine vasotocin and catecholamines in liver of the axolotl"; <i>J. Endocr.</i> , 109 (1986), pp. 75-84.	
XPL	A95	RIBEIRO et al.; "Pirrolidoncarbossilato Di Arginina E Lisina Nell'Anziano"; <i>Acta Gerontol.</i> 36 fasc. 1-2; 69-76 (1986).	
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XPL	A98	RADOMSKI et al.; "Comparative pharmacology of endothelium-derived relaxing factor, nitric oxide and prostacyclin in platelets"; <i>British J. Pharmac.</i> ; Vol. 92, pp. 181-187 (1987).	

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Examiner Signature	Jeffrey E. Russel	Date Considered	September 7, 2004
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Sheet 5 of 13

## Complete if Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number 080618-0237

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<i>JR</i>	A99	HENRIKSON et al.; "Separation and Identification of Two Components of an Estrogen-Responsive, Calcium-Dependent Arginine Esteropeptidase"; <i>J. Steroid Biochem.</i> , Vol. 24, No. 2; pp. 189-196 (1987).	
<i>JR</i>	A100	ANDREWS et al.; "Low-density lipoproteins inhibit endothelium-dependent relaxation in rabbit aorta"; <i>Nature</i> , Vol. 327, 21 (05-87), pp. 237-39.	
<i>JR</i>	A101	SAITO et al.; "Metabolic and Immune Effects of Dietary Arginine Supplementation After Burn"; <i>Arch. Surgery</i> (07-1987) 122:784-89.	
<i>JR</i>	A102	JOHANSSON et al.; "The actions of arginine and glucose on glucagon secretion are mediated by opposite effects on cytoplasmic Ca <sup>2+</sup> "; <i>Biomedical and Biophysical Research Communications</i> , Vol. 147, No. 1 (08-31-87), pp. 309-14.	
<i>JR</i>	A103	ISHIKAWA et al.; "Arginine Vasopressin Increases Cellular Free Calcium Concentration and Adenosine 3'-5'-Monophosphate Production in Rat Renal Papillary Collecting Tubule Cells in Culture"; <i>Endocrinology</i> , Vol. 123, No. 3 (1988), pp. 1376-84.	
<i>JR</i>	A104	PALMER et al.; "Vascular endothelial cells synthesize nitric oxide from L-arginine"; <i>Nature</i> Vol. 333, No. 16 (06-88). <i>Biochem. Biophys. Res. Comm.</i> , 153(3):1251-1256 (6-30-1988)	
<i>JR</i>	A105	YAMAMOTO et al.; "Videomicroscopic Demonstration of Defective Cholinergic Arteriolar Vasodilation in Atherosclerotic Rabbit"; <i>J. Clin. Invest.</i> , Vol. 81, pp. 1752-58 (06-1988).	
<i>JR</i>	A106	PALMER et al.; <i>Biochem and Biophys Res Comm</i> ; Vol. 153, No. 3, (06-30-88), pp. 1251-56.	
<i>JR</i>	A107	DALY et al.; "Immune and Metabolic Effects of Arginine in the Surgical Patient"; <i>Ann. Surg.</i> (10-1988) 208(4):512-23	
<i>JR</i>	A108	PIQUE et al.; "The vasodilator role of endogenous nitric oxide in the rat gastric microcirculation"; <i>European Journal of Pharmacology</i> , Vol. 174 (1989), pp. 293-96.	
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<i>JR</i>	A114	IGNARRO et al.; "Basic Polyamino Acids Rich in Arginine, Lysine or Ornithine Cause Both Enhancement of and Refractoriness to Formation of Endothelium-Derived Nitric Oxide in Pulmonary Artery and Vein"; <i>Circulation Research</i> , Vol. 64, No. 2 (02-1989), pp. 315-29.	

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*Jeffrey E. Russel*

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<b>Application Number</b>	10/618,835
<b>Filing Date</b>	07/15/2003
<b>First Named Inventor</b>	John P. Cooke
<b>Group Art Unit</b>	1654
<b>Examiner Name</b>	J. Russel

Attorney Docket Number 080618-0237

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JR	A116	REES et al.; "Role of endothelium-derived nitric oxide in the regulation of blood pressure"; <i>Proc. Natl. Acad. Sci.</i> (05-1989), 86:3375-78.	
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JR	A127	MONCADA et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 1 – Introduction"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 1-4.	
JR	A128	LEVI et al.; "Nitric Oxide From L-Arginine A Bioregulatory system – Chapter 4 – Evidence that L-arginine is the biosynthetic precursor of vascular and cardiac nitric oxide"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 35-44.	
JR	A129	SCHRÖDER et al.; "Nitric Oxide From L-Arginine A Bioregulatory system - Chapter 6 - L-Arginine potentiates and N <sup>G</sup> -monomethyl-L-arginine inhibits calcium ionophore-induced cyclic GMP stimulation in porcine aortic endothelial cells," <i>Elsevier Science Publishers B.V.</i> (1990), pp. 55-59.	
JR	A130	MONCADA et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 11 – Endothelium-derived nitric oxide in human arteries and veins," <i>Elsevier Science Publishers B.V.</i> (1990), pp. 89-93.	

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Date Submitted: April 19, 2004 <i>(use as many sheets as necessary)</i>				<b>Filing Date</b>	07/15/2003
				<b>First Named Inventor</b>	John P. Cooke
				<b>Group Art Unit</b>	1654
				<b>Examiner Name</b>	J. Russel
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JRL	A131	VALLANCE et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 12 – Endothelium-dependent responses and nitric oxide production in human vasculature in vivo"; Elsevier Science Publishers B.V. (1990), pp. 95-99			T <sup>6</sup>
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				<b>Attorney Docket Number</b>	080618-0237

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	A147	MILYUTINA et al.; "Antiradical and Antioxidative Effect of Arginine and Its Influence on Lipid Peroxidation Activity During Hypoxia"; <i>Bull. Exp. Biol. And Medicine</i> (1991), 110(9):1198-1200.			T <sup>6</sup>
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	A160	EFRON et al.; "Nitric oxide generation from L-arginine is required for optimal human peripheral blood lymphocyte DNA synthesis"; <i>Surgery</i> (08-1991), 110:327-34.			
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				<b>Application Number</b>	10/618,835
Date Submitted: April 19, 2004				<b>Filing Date</b>	07/15/2003
(use as many sheets as necessary)				<b>First Named Inventor</b>	John P. Cooke
Sheet	9	of	13	<b>Group Art Unit</b>	1654
				<b>Examiner Name</b>	J. Russel
				<b>Attorney Docket Number</b>	080618-0237

OTHER - NON PATENT LITERATURE DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.				T <sup>2</sup>
	A164	HISHIKAWA et al.; <i>Japanese Heart Journal</i> 33:41-48 (1-1992).				
	A165	HATTON et al.; "Arginine vasopressin mobilised intracellular calcium via V <sub>1</sub> -receptor activation in astrocytes (pituitary) cultured from adult rat neural lobes"; <i>Brain research</i> , Vol. 588 (1992), pp. 75-83.				
	A166	BUCHMÜLLER-ROUILLER et al.; "Macrophage activation for intracellular killing as induced by a Ca <sup>2+</sup> ionophore"; <i>Biochem J.</i> ; Vol. 284 (1992), pp. 387-92.				
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	A168	COOKE; "Endothelium-Derived Factors and Peripheral Vascular Disease"; <i>Cardiovascular Clinics</i> ; Vol. 22, No. 3 (1992), pp. 3-17.				
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	A171	BOEGEHOOLD; "Reduced Influence of Nitric Oxide on Arteriolar Tone in Hypertensive Dahl Rats" (1992), <i>Hypertension</i> 19:290-95.				
	A172	VANE et al.; "The Role of Chemical Mediators Released by the Endothelium in the Control of the Cardiovascular System" <i>Int J. Tiss. Reac.</i> XIV (2) (1992), pp. 55-64.				
	A173	RAJFER et al.; "Nitric Oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic neurotransmission"; <i>The New England Journal of Medicine</i> ; Vol. 326, No. 2 (01-09-92), pp. 90-94.				
	A174	JESEKICH et al.; "Reduced plasma L-arginine in hypercholesterolemia"; <i>The Lancet</i> , Vol. 339, (02-29-92), p. 561.				
	A175	MITCHELL et al.; "Native LDL inhibits the release of endothelial derived relaxing factor by reducing the activity of endothelial nitric oxide synthase"; <i>Journal of Vascular Research</i> (02-29-92), p. 169.				
	A176	KUO et al.; "Pathophysiological consequences of atherosclerosis extended into the coronary microcirculation. Restoration of endothelium-dependent response by L-arginine"; <i>Circulation Research</i> (03-1992), 70:465-76.				
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	A179	JANSSENS et al.; "Cloning and Expression of a cDNA Encoding Human Endothelium-derived Relaxing Factor-Nitric Oxide Synthase"; <i>The Journal of Biological Chemistry</i> , Vol. 267, No. 21 (07-25-92), pp. 14519-22.				

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Examiner Signature	Jeffrey E. Russel	Date Considered
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<b>First Named Inventor</b>	John P. Cooke
<b>Group Art Unit</b>	1654
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Attorney Docket Number 080618-0237

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XJL	A180	COOKE et al.; "Antiatherogenic effects of L-arginine in the hypercholesterolemic rabbit; <i>J. Clin. Invest.</i> (09-92), 90:1168-72.	
XJL	A181	HARRISON et al.; "Normal and Pathophysiologic Considerations of Endothelial Regulation of Vascular Tone and Their Relevance to Nitrate Therapy"; <i>Am. J. Cardiol.</i> (09-24-92), 70: <del>118-28</del> , 118 - 17B.	
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XJL	A189	KORBUT et al.; "Effect of L-Arginine on Plasminogen-Activator Inhibitor in Hypertensive Patients with Hypercholesterolemia"; <i>New Eng. Journal of Medicine</i> (01-28-93), pp. 328(4):287-88.	
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XJL	A194	BERDEAUX; "Nitric Oxide: an ubiquitous messenger"; <i>Fundam Clin Pharmacol</i> , Vol. 7 (05-25-93), pp. 401-11.	

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Examiner Signature	Jeffrey E. Russel	Date Considered	September 8, 2003
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<b>Filing Date</b>	07/15/2003
<b>First Named Inventor</b>	John P. Cooke
<b>Group Art Unit</b>	1654
<b>Examiner Name</b>	J. Russel

Attorney Docket Number 080618-0237

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	A207	WILLIAMS; "Another vanishing cure?", <i>Alternatives for the Health Conscious Individual</i> (11-94), 5(17): 129-35.	
	A208	WHITAKER (ed.); "An Amino Acid That Could Save Your Life"; <i>Health and Healing; Tomorrow's Medicine Today</i> (11-1994), 4(11):1-8.	
	A209	GILLIGAN et al.; "Contribution of Endothelium-Derived Nitric Oxide to Exercise-Induced Vasodilation"; <i>Circulation</i> (12-1994), 90:2853-58.	
	A210	HECKER et al.; "Mechanisms of Shear Stress-Dependent Endothelial Nitric Oxide Release: Cardiovascular Implications"; <i>Biochemical, Pharmacological, and clinical aspects of Nitric Oxide</i> (1995), pp. 49-59.	
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	A212	ALBINA et al.; "Chapter 7: Nitric Oxide"; <i>Amino Acid Metabolism and Therapy in Health and Nutritional Disease</i> (1995), pp. 99-115.	

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	A213	KEYSARY et al.; "The involvement of L-Arginine-Nitric Oxide Pathway in the Anti-Rickettsial Activity of Macrophagelike cells"; <i>Biochemical, Pharmacological, and clinical aspects of Nitric Oxide</i> (1995), pp. 111-14.	
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	A219	WHITAKER (ed.); "Advancing Years Need Not Impair Your Sex Life"; <i>Health and Healing; Tomorrow's Medicine Today</i> (09-1995), 5(9) 1,3,5,7.	
	A220	CHEMICAL ABSTRACT 126:190939 (1997), abstracting South Africa Patent No. 9410015, published November 8, 1995.	
	A221	HISHIKAWA, KEIICHI, M.D., et al., "Effect of Systemic L-Arginine Administration on Hemodynamics and Nitric Oxide Release in Man," <i>Japanese Heart Journal</i> , vol. 33, no. 1, January 1992, pp. 41-48.	
	A222	MONCADA, S., et al., "Nitric Oxide: Physiology, Pathophysiology, and Pharmacology," <i>Pharmacological Reviews</i> , vol. 43, no. 2, June 1991, pp. 109-142.	
	A223	GUDE, NM., et al., "Role of endothelium-derived nitric oxide in maintenance of low fetal vascular resistance in placenta," <i>The Lancet</i> , vol. 336, no. 8730, December 22-29, 1990, pp. 1589-1590.	
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	A227	HANSEN, JANICE I., M.D., et al., "Clinical Study of ArginMax, a Nutritional Supplement for the Enhancement of Female Sexual Function," <i>Journal of Women's Health &amp; Gender-Based Medicine</i> , vol. 11, no. 3, April 2002. (one page).	

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Date Considered

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<i>JRL</i>	A228	D. PEARSON and S. SHAW, <u>The Life Extension Companion</u> , Warner Books (1984), NY, pp. cover to cover (1325 pages total).	
<i>JRL</i>	A229	D. PEARSON and S. SHAW, <u>The Life Extension Companion</u> , Warner Books (1984), NY, pp. 461-62; 467-68; 485; 611-13; and 620.	
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<i>JRL</i>	A234	Derwent Abstract of EP 441119 A, 08/14/1991, "Use of L-arginine - to treat high vascular resistance disorders, e.g. hypertension and bronchial asthma," 2 pages.	
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<i>JRL</i>	A236	Derwent Abstract of EP 511118 A, 10/28/1992, "Use of lysine and arginine pyrrolidone carboxylate(s) as anti-oxidants - preferably with a phenolic derivative, e.g. tocopherol, in pharmaceutical and cosmetic compositions, particularly to protect skin from ageing," 2 pages.	
<i>JRL</i>	A237	Derwent Abstract of EP 546796 A, 06/16/1993, "Use of L-arginine - for treating and preventing atherosclerosis," 1 page.	
<i>JRL</i>	A238	Inpadoc Abstract of ZA 9410015 A, 11/08/1995, "A pharmaceutical composition," 1 page.	
<i>JRL</i>	A239	Derwent Abstract of WO 9318156 A, 09/16/1993, "Endothelial nitric oxide synthase and gene - which catalyses nitric oxide formation, for, e.g., inhibiting platelet aggregation or smooth muscle cell proliferation," 1 page.	
<i>JRL</i>	A240	Derwent Abstract of JP 7163269A, 06/27/1995, "Bearing cattle of special gender - by controlling amount of alginine and calcium in feedstuff," 1 page.	
<i>JRL</i>	A241	Derwent Abstract of FR 2547501 A, 12/21/1984, "Arginine carbonate, citric acid compositions - giving effervescent agents for tablets, free from alkaline earth metals," 1 page.	

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Examiner Signature	Jeffrey E. Russel	Date Considered	September 7, 2004
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		<b>Complete if Known</b>	
Date Submitted: May 19, 2004 (use as many sheets as necessary)		Application Number	10/618,835
		Filing Date	7/15/2003
		First Named Inventor	John P. Cooke
		Group Art Unit	1654
		Examiner Name	J. Russel
Sheet	1	of	1
		Attorney Docket Number	080618-0237

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
XJL	F1	4,900,566		Howard	2/13/1990	426/172
XJL	F2	5,106,836		Clemens et al.	4/21/1992	514/21

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>				
XJL	F3	EP	0511587	A1	Takeda Chemical Industries, Ltd.	11/04/1992	

**NON PATENT LITERATURE DOCUMENTS**

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XJL	F4	JP60094075A, AJINOMOTO KK; Dialog Japanese Abstract (1 pg.) (May 27, 1985).						
XJL	F5	JP61254162A, KAMEHIKO MOGI, Dialog Japanese Abstract (1 pg.) (Nov. 11, 1986)						
XJL	F6	JP59210872A, AJINOMOTO KK, Dialog Japanese Abstract (1 pg.) (Nov. 29, 1984)						
XJL	F7	JP61215323A, OTSUKA PHARM CO., Dialog Japanese Abstract (1 pg.) (Sept. 25, 1986)						
XJL	F8	JP60049764A, AJINOMOTO KK, Dialog Japanese Abstract (1 pg.) (March 19, 1985)						
XJL	F9	European Search Report dated 7/31/03 for EP Application No. 107776.2						

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STATEMENT BY APPLICANT

Date Submitted: May 21, 2004

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Sheet 1 of 15

		Complete if Known	
		Application Number	10/618,835
		Filing Date	07/15/2003
		First Named Inventor	John P. Cooke
		Group Art Unit	1654
		Examiner Name	J. Russel
		Attorney Docket Number	080618-0237

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JKR	C1	2002/0091160	A1	COOKE, et al.	02-01-2002	541564
JKR	C2	5,026,721		DUDRICK, et al.	06-25-1991	
JKR	C3	5,028,627		KILBOURN, et al.	07-02-1991	
JKR	C4	6,117,872		MAXWELL, et al.	09-12-2000	
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JKR	C6	6,552,074		KIMOTO, et al.	04-22-2003	
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JKR	C8	EP	0 259 167 A2	Millman	03-09-1988	
JKR	C9	EP	0 511 118 A1	N'Guyen	10-28-1992	
JKR	C10	EP	511 587 A1	Moriyama et al.	11-04-1992	
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JKR	C12	WO	98/18491	Burgstiner	05-07-1998	
JKR	C13	ZA	9410015 A	Davis et al.	11-08-1995	
JKR	C14	FR	2 507 892	Brugioni et al.	12-24-1982	
JKR	C14a	GB	2 100 982	Brugioni et al.	06-22-1982	
JKR	C15	WO	85/00517	Niebes et al.	02-14-1985	

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JKR	C16	Adams et al., "Oral L-arginine improves endothelium-dependent dilatation and reduces monocyte adhesion to endothelial cells in young men with coronary artery disease" <i>Atherosclerosis</i> , 1997, 129(2):261-69.	
JKR	C17	Adams et al., "Cigarette smoking is associated with increased human monocyte adhesion to endothelial cells: reversibility with oral L-arginine but not vitamin C," <i>J. Amer. Coll. Cardiol.</i> , 1997, 29(3):491-97.	

Examiner Signature

Jeffrey E. Russel

Date Considered

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Sheet

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15

## Complete if Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number 080618-0237

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<i>JR</i>	C18	Aimasheva et al., "Donor of nitric oxide improves, while NO-synthase inhibitor impairs resistance and adaptation to strenuous physical exercise," <i>Bulletin of Exp. Biol. and Med.</i> , 1998, 4:336-339.	
<i>JR</i>	C19	Aisaka et al., "N <sup>G</sup> -monomethyl-L-arginine, an inhibitor of endothelium-derived nitric oxide synthesis, abbreviates acetylcholine-induced vasodilatation in the guinea-pig" in <i>Nitric Oxide from L-arginine: a Bioregulatory System</i> (S. Moncada and E.A. Higgs, eds.), 1990, Chapter 40, pp. 379-384.	
<i>JR</i>	C20	Aisaka et al., "Modulation of cardiovascular function by L-arginine-derived nitric oxide" <i>Frontiers and new horizons in amino acid research</i> (K. Takai, ed.), 1992, 437-442.	
<i>JR</i>	C21	Aisaka et al., "Regulation of vascular resistance by L-arginine-derived nitric oxide," <i>J. Pharmacobio-Dyn.</i> , 1992, 15:s-60.	
<i>JR</i>	C22	Alba-Roth et al., "Arginine stimulates growth hormone secretion by suppressing endogenous somatostatin secretion," <i>J. Clin. Endocrinol. Metab.</i> , 1988, 67(6):1186-89.	
<i>JR</i>	C23	Amrani et al., "Role of basal release of nitric oxide on coronary flow and mechanical performance of the isolated rat heart," <i>J. Physiol.</i> , 1992, 456:681-87.	
<i>JR</i>	C24	Aoyama et al., "Effects on liver and serum lipids of dietary supplements of methionine and excess lysine given to previously-starved rats," <i>British J. Nutr.</i> , 1983, 50(3):627-36.	
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<i>JR</i>	C27	Barbul A., "Arginine and immune function," 1999, <i>Nutr.</i> 6(1)53-62. <i>1970</i>	
<i>JR</i>	C28	Barbul et al., "Arginine: a thymotropic and wound-healing promoting agent," 1977, <i>Surg. Forum.</i> 28:101-103.	
<i>JR</i>	C29	Barclay et al., "The role of blood flow in limiting maximal metabolic rate in muscle," 1975, <i>Med Sci Sports.</i> 7(2):116-119.	
<i>JR</i>	C30	Baumier et al., "Arginine: new and exciting developments for an 'old' amino acid," 1996, <i>Biomed. Environ. Sci.</i> 9(2-3):296-315.	
<i>JR</i>	C31	Bellamy et al., "Oral L-arginine improves exercise tolerance and flow-related endothelial dysfunction in microvascular angina," 1996, Abstract No. 2478, <i>Suppl. Circulation</i> 94(8):I-425.	

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*Jeffrey E. Russel*

Date Considered

*September 7, 2004*

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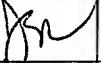
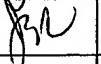
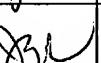
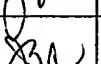
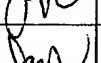
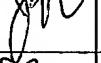
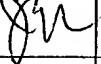
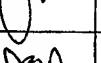
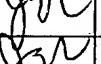
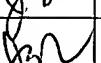
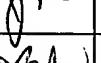
Sheet 3 of 15

## Complete if Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number 080618-0237

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	C32	Bissell, "Porphyria," Textbook of Medicine (ed. Wyngaarden and Smith), W.B. Saunders Co., Harcourt Brace Jovanovich Inc. Philadelphia, 1988, pp. 1182-89.	
	C33	Blomqvist, "Cardiovascular adaptations to physical training," 1983, Annu. Rev. Physiol. 45:169-89.	
	C34	Blum et al., "Oral L-arginine in patients with coronary artery disease on medical management," 2000, Circulation 101:2160-64.	
	C35	Bode-Boger et al., "Exercise increases systemic nitric oxide production in men," 1994, Cardiovasc. Risk. 1(2):173-78.	
	C36	Bode-Boger et al., "L-arginine infusion decreases peripheral arterial resistance and inhibits platelet aggregation in healthy subjects," 1994, Clin. Sci. (Lond) 87(3):303-10.	
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Sheet 4 of 15

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<i>JR</i>	C45	Castillo et al., "Dietary arginine uptake by the splanchnic region in adult humans" Am J Physiol. 1993, 65(4 Pt 1):E532-39.	
<i>JR</i>	C46	Castillo et al., "Splanchnic metabolism of dietary arginine in relation to nitric oxide synthesis in normal adult man" Proc. Natl. Acad. Sci. USA 1993, 90(1):193-97.	
<i>JR</i>	C47	Castillo et al., "Plasma arginine and citrulline kinetics in adults given adequate and arginine-free diets" Proc. Natl. Acad. Sci. USA 1993, 90:7749-53.	
<i>JR</i>	C48	Castillo et al., "Plasma arginine kinetics in adult man: response to an arginine-free diet" Metabolism 1994, 43(1):114-22.	
<i>JR</i>	C49	Ceremuzkynski et al., "L-arginine improves exercise capacity in patients with stable angina" Supplement to J. of Am. College of Cardiology, 1997, 29(2): Supp. A. Abstract 962-94.	
<i>JR</i>	C50	Ceremuzynski et al., "Effect of supplemental oral L-arginine on exercise capacity in patients with stable angina pectoris" Am. J. Cardiol. 1997, 80(3):331-33.	
<i>JR</i>	C51	Chauhan et al., "Aging-associated endothelial dysfunction in humans is reversed by L-arginine" J. Amer. Coll Cardiol. 1996, 28(7):1796-1804.	
<i>JR</i>	C52	Chen et al., "L-arginine prevents hypertension in salt-sensitive (SS/Jr) Dahl/Rapp rats" Clinical Research 1991, 39:379A.	
<i>JR</i>	C53	Chen et al., "Hypertensive Nephrosclerosis in the Dahl/Rapp Rat: Initial Sites of Injury and Effect of Dietary L-Arginine Supplementation" Laboratory Investigation 1993, 68(2):174-184.	
<i>JR</i>	C54	Chen et al., "Effects of chronic treatment with L-arginine on atherosclerosis in ApoE knockout and ApoE/inducible NO synthase double-knockout mice" Arterioscler. Thromb. Vasc. Biol. 2003, 23:97-103.	
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<i>JR</i>	C56	Chester et al., "Low basal and stimulated release of nitric oxide in atherosclerotic epicardial coronary arteries" Lancet 1990, 336(8720):897-900.	
<i>JR</i>	C57	Chester et al., "The role of nitric oxide in mediating endothelium dependent relaxations in the human epicardial coronary artery" Int J Cardiol. 1990, 29(3):305-09.	

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*Jeffrey E. Russel*

Date Considered

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
Date Submitted: May 21, 2004				Filing Date	07/15/2003
(use as many sheets as necessary)				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	5	of	15	Attorney Docket Number	
080618-0237					

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<i>JR</i>	C58	Church et al., "Hypertension and renal impairment as complications of acute porphyria" Nephrol Dial Transplant. 1992, 7(10):986-90.			
<i>JR</i>	C59	Cooke et al., "Endothelial dysfunction in hypercholesterolemia is corrected by L-arginine" Basic Res Cardiol., 1991, 86 Suppl 2:173-81.			
<i>JR</i>	C60	Cooke J.P., "A peculiar result and a fanciful hypothesis regarding L-arginine" Atheroscler. Thromb. Vasc. Biol. 2003, 23:1128-31.			
<i>JR</i>	C61	Creager et al., "L-arginine improves endothelium-dependent vasodilation in hypercholesterolemic humans" Supplement to Circulation 1990, 82:III-346, 1248-1253.			
<i>JR</i>	C62	Cynober et al., "Arginine metabolism in mammals" J. Nutr. Biochem. 1995, 6:402-13.			
<i>JR</i>	C63	Davies et al., "Combination therapy of cholesterol reduction and L-arginine supplementation controls accelerated vein graft atheroma" Ann. Vasc. Surg. 1999, 13(5):484-93.			
<i>JR</i>	C64	de Graaf JC et al., "Nitric oxide functions as an inhibitor of platelet adhesion under flow conditions". Circulation 1992, (6):2284-90.			
<i>JR</i>	C65	Deguchi et al., "L-Arginine identified as an endogenous activator for soluble guanylate cyclase from neuroblastoma cells". J. Biol. Chem. 1982, 257(17):10147-51.			
<i>JR</i>	C66	Dhanakoti et al., "Net renal arginine flux in rats is not affected by dietary arginine or dietary protein intake" Nutrient Metabolism 1992, 122(5):1127-34.			
<i>JR</i>	C67	Dubois-Rande, Jean-Luc et al., "L-arginine improves endothelium-dependent relaxation of conductance and resistance coronary arteries in coronary artery disease" J. of Cardio Pharm. 1992, 20(Suppl. 12):S211-S213.			
<i>JR</i>	C68	Edmonds et al., "Urea cycle metabolism: effects of supplemental ornithine or citrulline on performance, tissue amino acid concentrations and enzymatic activity in young pigs fed arginine-deficient diets" Anim. Sci. 1987, 65(3):706-16.			
<i>JR</i>	C69	Eklund et al., "Effects of the Source of Dietary Protein on Serum Lower Density Lipoprotein (VLDL + LDL) and Serum Tocopherol Levels in Female Rats" J. Nutr. 1980, 110(12):2321-35.			
<i>JR</i>	C70	Elder et al., "The acute porphyrias" Lancet. 1997 349(9065):1613-17.			
<i>JR</i>	C71	Elder et al., "Treatment of acute porphyria" Hosp Med. 2001, 62(7):422-25.			

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<i>JR</i>	C72	Feng Q., et al., "Endothelium-derived relaxing factor (EDRF) and nitric oxide (NO). I. Physiology, pharmacology and pathophysiological implications" Clin. Physiol. 1990, (5):407-26.			
<i>JR</i>	C73	Freiman et al., "Atherosclerosis impairs endothelium-dependent vascular relaxation to acetylcholine and thrombin in primates," Circ Res. 1986, 58(6):783-89.			
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<i>JR</i>	C75	Furchtgott et al., "Interactions of endothelial cells and smooth muscle cells of arteries" Chest. 1985, 88(4 Suppl):210S-213S.			
<i>JR</i>	C76	Martin et al., "Depression of contractile responses in rat aorta by spontaneously released endothelium-derived relaxing factor" Pharmacol. Exp. Ther. 1986, 237(2):529-38.			
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<i>JR</i>	C78	Furchtgott et al., "Evidence supporting the proposal that endothelium-derived relaxing factor is nitric oxide" Thrombosis Research 1987, Supp. VII:5.			
<i>JR</i>	C79	Furchtgott et al., "Evidence that the endothelium-derived relaxing factor of rabbit aorta is nitric oxide" Dept. of Pharmacology, SUNY Health Science Center at Brooklyn, NY, 1988, 77-84.			
<i>JR</i>	C80	Furchtgott et al., "Endothelium-derived relaxing and contracting factors" FASEB J. 1989, 3(9):2007-18.			
<i>JR</i>	C81	Furchtgott et al., "Interactions of superoxide and hydrogen peroxide with nitric oxide and EDRF in the regulation of vascular tone" Endothelium-Derived Factors and Vascular Functions (T. Masaki, ed.), 1994, pp. 3-11.			
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<i>JR</i>	C83	Furchtgott RF, "The pharmacology of vascular smooth muscle" Pharmacol Rev. 1955, 7(2):183-265.			
<i>JR</i>	C84	Furchtgott RF, "A research trail over half a century" Ann. Rev. Pharmacol. Toxicol. 1995, 35:1-27.			
<i>JR</i>	C85	Furchtgott RE, Bhadrakom S, "Reactions of strips of rabbit aorta to epinephrine, isopropylarterenol, sodium nitrite and other drugs" J. Pharmacol. Exp. Ther. 1953, 108(2):129-43.			

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<i>JR</i>	C86	Furchtgott, RF, "The role of endothelium in the responses of vascular smooth muscle to drugs" Ann. Rev. Pharmacol. Toxicol. 1984, 24:175-97.				
<i>JR</i>	C87	Furchtgott, RF, "The 1989 Ulf von Euler lecture. Studies on endothelium-dependent vasodilation and the endothelium-derived relaxing factor" Acta Physiol. Scand. 1990, 139(2):257-70.				
<i>JR</i>	C88	Furchtgott, RF, "Introduction to EDRF Research" J. Cardiovascular Pharmacology Vol. 22, Supplement 7, 1993, pp. S1-S2.				
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<i>JR</i>	C90	Furchtgott, RF, "The Discovery of Endothelium-Derived Relaxing Factor and Its Importance in the Identification of Nitric Oxide" JAMA 1996, 276(14) 1186-88.				
<i>JR</i>	C91	Furchtgott, RF, "Discovery of endothelium-derived relaxing factor and its identification as nitric oxide" Endothelium, Nitric Oxide, and Atherosclerosis (Panza et al., eds.), 1999, Chapter 1, pp. 3-11.				
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<i>JR</i>	C94	Gordon, "The acute porphyrias" Brain Dev. 1999, 21(6):373-77.				
<i>JR</i>	C95	Grossman et al., "The Effects of External Calcium Concentration on the Distribution and Exchange of Calcium in Resting and Beating Guinea-Pig Auricles" J. Pharmacol. Exp. Ther. 1964, 143:107-19.				
<i>JR</i>	C96	Grossman et al., "The Effects of Frequency of Stimulation and Calcium Concentration on CA45 Exchange and Contractility on the Isolated Guinea-Pig Auricle" J. Pharmacol. Exp. Ther. 1964, 143:120-30.				
<i>JR</i>	C97	Grossman et al., "The Effects of Various Drugs on Calcium Exchange in the Isolated Guinea-Pig Left Auricle" J. Pharmacol. Exp. Ther. 1964, 145:162-72.				
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Sheet	8	of	15	Attorney Docket Number	080618-0237
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<i>JR</i>	C99	Henderson, (St Cyres lecture) "Endothelium in control," Br. Heart J. 1991, 65(3):116-25.	
<i>JR</i>	C100	Hishikawa et al., "L-arginine-induced hypertension" Lancet 1991, 337:683-84.	
<i>JR</i>	C101	Hishikawa et al., "L-arginine as an antihypertensive agent" J. of Cardio. Pharm. 1992, 22 (Suppl 12): S196-7.	
<i>JR</i>	C102	Hurson et al., "Metabolic effects of arginine in a healthy elderly population" JPEN J. Parenter. Enteral. Nutr. 1995, 19(3):227-30.	
<i>JR</i>	C103	Ignarro et al., "Alteration of endothelium-dependent arterial relaxation by arginine analogs and arginine depletion" Endothelium-Derived Relaxing Factors (Rubanyi et al., eds.), 1990, pp. 64-74.	
<i>JR</i>	C104	Ignarro, "Endothelium-derived nitric oxide: actions and properties" FASEB J. 1989, 3(1):31-36.	
<i>JR</i>	C105	Ignarro, "Biosynthesis and metabolism of endothelium-derived nitric oxide" Annu Rev Pharmacol. Toxicol. 1990, 30:535-60.	
<i>JR</i>	C106	Ignarro, "Nitric oxide. A novel signal transduction mechanism for transcellular communication" Hypertension 1990, 16(5):477-83.	
<i>JR</i>	C107	Ikeda et al., "Dietary N <sup>G</sup> -nitro-arginine induces sustained hypertension in normotensive Wistar-Kyoto rats" Clin. and Exper. Pharmacol. and Physiol. 1992, 19:583-86.	
<i>JR</i>	C108	Kauppinen, "Management of the acute porphyrias" Photodermatol. Photoimmunol. Photomed. 1988, 14(2):48-51.	
<i>JR</i>	C109	Kilbourn et al., "Reversal of endotoxin-mediated shock by NG-methyl-L-arginine, an inhibitor of nitric oxide synthesis" Biochem. Biophys. Res. Commun. 1990, 15;172(3):1132-38.	
<i>JR</i>	C110	Kilbourn et al., "Inhibition of interleukin-1- $\beta$ -induced nitric oxide synthase in vascular smooth muscle and full reversal of interleukin-1-alpha-induced hypotension by N omega-amino-L-arginine" J. Natl. Cancer Inst. 1992, 84(13):1008-16.	
<i>JR</i>	C111	Koifman et al., "Improvement of cardiac performance by intravenous infusion of L-arginine in patients with moderate congestive heart failure" J. Am. Coll. Cardiol. 26(5):1251-56. (Nov. 1995),	
<i>JR</i>	C112	Kordac, et al., "Changes of myocardial functions in acute hepatic porphyrias. Role of heme arginate administration," Annals of Medicine 1989, 21(4):273-76.	

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JR	C114	Lane, P., et al., "Cell signaling by nitric oxide," Semin Nephrol. 1999, 19(3):215-29.	
JR	C115	Leclercq-Meyer V., et al., "Calcium dependency of glucagon release: its modulation by nutritional factors," Am J Physiol 1979, 236(2):E98-104.	
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JR	C117	Levere, et al., "Effect of heme arginate administration on blood pressure in spontaneously hypertensive rats," Clin Invest. 1990, 86(1):213-9.	
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JR	C119	Lip, et al., "The acute porphyrias," Br. J. Clin. Pract. 1993, 47(1):38-43.	
JR	C120	Luscher, et al., "Endothelium-dependent responses in carotid and renal arteries of normotensive and hypertensive rats" Hypertension. 1988 11(6 Pt 2):573-8.	
JR	C121	Marcelin et al., "Modulating Role of Nitric Oxide Pathway on the Synthesis of PGI <sub>2</sub> in Rat Endothelial Cells in Culture," Hypertension 1999, 33(4):1297.	
JR	C122	Marin et al., "Role of endothelium-formed nitric oxide on vascular responses" Gen Pharmacol. 1990 21(5):575-87.	
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<i>JR</i>	C126	Martasek et al., "Hemin and L-arginine regulation of blood pressure in spontaneous hypertensive rats" J. Am. Soc. Nephrol. 1991, 2(6):1078-84.	
<i>JR</i>	C127	Martin et al., "Phosphodiesterase inhibitors induce endothelium-dependent relaxation of rat and rabbit aorta by potentiating the effects of spontaneously released endothelium-derived relaxing factor" J. Pharmacol. Exp. Ther. 1986, 237(2):539-47.	
<i>JR</i>	C128	Maxwell et al., "Cardiovascular effects of L-arginine" Curr. Opin. Nephrol. Hypertens. 1998, 7:63-70 (review).	
<i>JR</i>	C129	Maxwell et al., "Limb blood flow during exercise is dependent on nitric oxide" Circulation 1998, 98(4):369-74.	
<i>JR</i>	C130	Maxwell et al., "Hypercholesterolemia impairs exercise capacity: Role of nitric oxide" (Stanford University draft), 1998, pp. 1-23 and 33-34.	
<i>JR</i>	C131	Maxwell et al., "Nutritional therapy for peripheral arterial disease: a double-blind, placebo-controlled, randomized trial of HeartBar®" Vasc. Med. 2000, 5:11-19.	
<i>JR</i>	C132	Maxwell et al., "L-arginine enhances aerobic exercise capacity in association with augmented nitric oxide production" J. Appl. Physiol. 2001, 90(3):933-38.	
<i>JR</i>	C133	Merimee et al., "Arginine-initiated release of human growth hormone. Factors modifying the response in normal man" New Engl. J. Med. 1969, 280(24):1434-38.	
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<i>JR</i>	C136	Moncada and Higgs, "Endogenous nitric oxide: physiology, pathology and clinical relevance" Eur. J. Clin. Invest. 1991, 21(4):361-74.	
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<i>JR</i>	C138	Moncada S, et al., "Biosynthesis of nitric oxide from L-arginine. A pathway for the regulation of cell function and communication" Biochem Pharmacol. 1989, 38(11):1709-15.	
<i>JR</i>	C139	Moncada S, et al., "The biological significance of nitric oxide formation from L-arginine" Biochem. Soc. Trans. 1989, vol. 17(4):642-44.	

Examiner Signature

*Jeffrey C. Russell*

Date Considered

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
Date Submitted: May 21, 2004				Filing Date	07/15/2003
(use as many sheets as necessary)				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	11	of	15	Attorney Docket Number	080618-0237

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
JR	C140	Moncada et al., "International Union of Pharmacology Nomenclature in Nitric Oxide Research" Pharmacol. Rev. 1997, 49(2):137-42.	
JR	C141	Moncada, "The first Robert Furchtgott lecture: from endothelium-dependent relaxation to the L-arginine:NO pathway" Blood Vessels 1990, 27(2-5):208-17.	
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JR	C144	Niebauer et al., "Impaired aerobic capacity in hypercholesterolemic mice: partial reversal by exercise training" Am. J. Physiol. 1999, 276:H1346-H1354.	
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JR	C149	Palmer et al., "Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor" Nature 1987, 327:524-26.	
JR	C150	Palmer et al., "The biological significance of nitric oxide formation from L-arginine" Biochem. Soc. Trans. 1989, 17(4):642-44.	
JR	C151	Park et al., "Effects of dietary protein and amino acids on the metabolism of cholesterol-carrying lipoproteins in rats" J. Nutr. 1982, 112(10):1892-98.	
JR	C152	Park et al., "Nitric oxide is a mediator of hypoxic coronary vasodilatation. Relation to adenosine and cyclooxygenase-derived metabolites" Circ. Res. 1992, 71(4):992-1001.	
JR	C153	Patel et al., "L-arginine administration normalizes pressure natriuresis in hypertensive Dahl rats" Hypertension 1993, 22(6):863-69.	

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Date Submitted: May 21, 2004

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Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number

080618-0237

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<i>JR</i>	C155	Pizcueta et al., "Effects of inhibiting nitric oxide biosynthesis on the systemic and splanchnic circulation of rats with portal hypertension" Br J Pharmacol. 1992, 105(1):184-90.	
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<i>JR</i>	C157	Preli et al., "Vascular effects of dietary L-arginine supplementation" Atherosclerosis 2002, 162:1-15.	
<i>JR</i>	C158	Radomski et al., "An L-arginine/nitric oxide pathway present in human platelets regulates aggregation" Proc Natl Acad Sci USA. 1990, 87(13):5193-97.	
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<i>JR</i>	C162	Reynolds et al., "Immunomodulatory mechanisms of arginine" Surgery 1988, 104(2):142-51.	
<i>JR</i>	C163	Rubanyi et al., "Superoxide anions and hyperoxia inactivate endothelium-derived relaxing factor" Am. J. Physiol. 1986, 250:H822-H827.	
<i>JR</i>	C164	Rubanyi, "The role of endothelium in cardiovascular homeostasis and diseases" J. of Cardio, Pharm. 1993, 22 (Suppl.) S1-S14.	
<i>JR</i>	C165	Sakuma et al., "Identification of arginine as a precursor of endothelium-derived relaxing factor" Proc. Natl. Acad. Sci. USA 1988, 85(22):8664-67.	
<i>JR</i>	C166	Sakuma et al., "L-Arginine is a Precursor of Endothelium-Derived Relaxing Factor in Various Animal Species and Vascular Beds" in Nitric Oxide from L-Arginine: A Bioregulatory System (Moncada and Higgs, eds.) 1990, Chapter 49, pp. 445-49.	
<i>JR</i>	C167	Sanchez et al., "Testing a mechanism of control in human cholesterol metabolism: relation of arginine and glycine to insulin and glucagon" Atherosclerosis 1988, 71:87-92.	

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STATEMENT BY APPLICANT

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Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Sheet 13 of 15

Attorney Docket Number 080618-0237

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<i>JR</i>	C168	Sanchez et al., "Plasma amino acids and the insulin/glucagon ratio as an explanation for the dietary protein modulation of atherosclerosis" Medical Hypotheses 1991, 35:324-29.	
<i>JR</i>	C169	Schaffer et al., "Nitric oxide regulates wound healing" J. Surg. Res. 1996, 63(1):237-40.	
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<i>JR</i>	C177	Steinsland OS et al., "Biphasic vasoconstriction of the rabbit ear artery" Circ. Res. 1973, (1):49-58.	
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<i>JR</i>	C180	Thadani et al., "Diagnosis and management of porphyria" BMJ. 2000, 320(7250):1647-51.	
<i>JR</i>	C181	Thomas G, et al., "Vasodilatory properties of mono-L-arginine-containing compounds" Biochem Biophys Res Commun. 1988, 154(1):332-38.	

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*Jeffrey B. Russel*

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*September 7, 2004*

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## Complete If Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel

Attorney Docket Number 080618-0237

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JRN	C182	Togashi et al., "A central nervous system action of nitric oxide in blood pressure regulation" J. Pharmacol. Exp. Ther. 1992, 262(1):343-47.	
JRN	C183	Umans et al., "Nitric oxide in the regulation of blood flow and arterial pressure" Annu. Rev. Physiol. 1995, 57:771-790.	
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JRN	C185	Vallance et al., "Effects of endothelium-derived nitric oxide on peripheral arteriolar tone in man" Lancet 1989, 2(8670):997-1000.	
JRN	C186	Vane et al., (Mechanisms of disease) "Regulatory functions of the vascular endothelium" New England J. Med. 1990, 323:27-36.	
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JRN	C189	Vane, "Control of the circulation by endothelial mediators," Inaugural G.B. West Memorial Lecture, Int. Arch. Allergy Immunol. 1993, 101(4):333-45.	
JRN	C190	Vanhoutte et al., "Modulation of vascular smooth muscle contraction by the endothelium" Annu. Rev. Physiol. 1986, 48:307-20.	
JRN	C191	Venho et al., "Arginine intake, blood pressure, and the incidence of acute coronary events in men: the Kuopio Ischaemic Heart Disease Risk Factor Study" Am. J. Clin. Nutr. 2002, 76:359-64.	
JRN	C192	Volin et al., "Heme arginate: effects on hemostasis" Blood 1988, 71(3):625-28.	
JRN	C193	von der Leyen HE, et al., "Gene therapy inhibiting neointimal vascular lesion: in vivo transfer of endothelial cell nitric oxide synthase gene" Proc. Natl. Acad. Sci. USA 1995 92(4):1137-41.	
JRN	C194	Waldman SA et al., "Biochemical mechanisms underlying vascular smooth muscle relaxation: the guanylate cyclase-cyclic GMP system" J Cardiovasc Pharmacol. 1988, 12 Suppl 5:S115-8.	
JRN	C195	Waller et al., "Conditions for synthesis of antioxidative arginine-xylose maillard reaction products" Synthesis of Antioxidative Products 1983, pp. 125-40.	

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Date Submitted: May 21, 2004 <i>(use as many sheets as necessary)</i>				Filing Date	07/15/2003
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Sheet	15	of	15	Attorney Docket Number	080618-0237

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<i>JR</i>	C197	Wascher, "Oral L-arginine supplementation in chronic heart failure" Circulation 1997, 95(6):1674-75.				
<i>JR</i>	C198	Wennmalm, "Endothelial nitric oxide and cardiovascular disease" J. Intern. Med. 1994, 235(4):317-27.				
<i>JR</i>	C199	Weyrich et al., "The Role of L-Arginine in Ameliorating Reperfusion Injury After Myocardial Ischemia in the Cat" Circulation 1992, 86(1):279-88.				
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<i>JR</i>	C201	Windmueller et al., "Source and fate of circulating citrulline" Am. J. Physiol. 1981 241(6):E473-80.				
<i>JR</i>	C202	Wu et al., "Arginine metabolism: nitric oxide and beyond" Biochem. J. 1998 336:1-17.				
<i>JR</i>	C203	Wu et al., "Arginine nutrition and cardiovascular function" Ann. Society Nutr. Sci. 2000, 130:2626-29. <i>J. Nutr.</i>				
<i>JR</i>	C204	Zeiher et al., "Modulation of coronary vasomotor tone in humans. Progressive endothelial dysfunction with different early stages of coronary atherosclerosis" Circulation 1991 83(2):391-401.				
<i>JR</i>	C205	Zeiher et al., "Endothelial Dysfunction of the Coronary Microvasculature Is Associated With Impaired Coronary Blood Flow Regulation in Patients With Early Atherosclerosis" Circulation 1991, 84(5):1984-92.				
<i>JR</i>	C206	Dialog Search Result for Normosang Synonyms. Chemsearch Database <i>(not dated)</i>				
<i>JR</i>	C207	European Porphyria Initiative, <a href="http://www.porphyria-europe.com">http://www.porphyria-europe.com</a> , selected pages <i>(2 - 13 - 2004)</i>				
<i>JR</i>	C208	Stedman's Medical Dictionary, The Williams and Wilkins Co. (23 <sup>rd</sup> Edition 1976), p. 1124.				

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Date Submitted: July 16, 2004				Application Number	10/618,835
(use as many sheets as necessary)				Filing Date	7/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
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FOREIGN PATENT DOCUMENTS						Class / Subclass	
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>8</sup>
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XJL	G19	WO	97/16983	THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY	05/15/1997	—	
XJL	G20	WO	95/24898	COMEDICUS, INCORPORATED	09/21/1995	—	
XJL	G21	WO	95/05866	CORTRAK MEDICAL INC.	03/02/1995	—	
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				<b>Application Number</b>	10/618,835
Date Submitted: July 16, 2004				<b>Filing Date</b>	7/15/2003
(use as many sheets as necessary)				<b>First Named Inventor</b>	John P. Cooke
				<b>Group Art Unit</b>	1654
				<b>Examiner Name</b>	J. Russel
Sheet	2	of	3	Attorney Docket Number	080618-0237

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Office <sup>3</sup>	Number <sup>4</sup>			

NON PATENT LITERATURE DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.				
GJL	G23	LEFER ET AL., "Role of Endothelium-derived Relaxing Factor as a Cardioprotective Agent in Myocardial Ischemia", <i>Basil, Karger</i> (1990), pp. 190-197.				T <sup>6</sup>
GJL	G24	IGNARRO ET AL., "Basic Polyamino Acids Rich in Arginine . . .," <i>Circ. Res.</i> (Feb. 1989), Vol. 64, No. 2, pp. 315-329.				
GJL	G25	ROCK ET AL., "L-arginyl-L-lysine and L-arginyl-L-arginine . . .," <i>Med. Sci. Res.</i> (1990), Vol. 18, pp. 165-166.				
GJL	G26	CAYATTE, Antonio J., et al., "Chronic Inhibition of Nitric Oxide Production Accelerates Neointima Formation and Impairs Endothelial Function in Hypercholesterolemic Rabbits," <i>Arteriosclerosis and Thrombosis</i> , Vol. 14, No. 5, 753-759 (May 1994).				
GJL	G27	DREXLER, Helmut, et al., "Effect of L-Arginine on Coronary Endothelial Function in Cardiac Transplant Recipients," <i>Circulation</i> , Vol. 89, No. 4, 1615-1623 (Apr. 1994).				
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GJL	G29	NARUSE, Kenshin, et al., "Long-Term Inhibition of NO Synthesis Promotes Atherosclerosis in the Hypercholesterolemic Rabbit Thoracic Aorta," <i>Arteriosclerosis and Thrombosis</i> , Vol. 14, No. 5, 746-752 (May 1994).				
GJL	G30	TSAO, Philip S., et al., "L-Arginine Attenuates Platelet Reactivity in Hypercholesterolemic Rabbits," <i>Arteriosclerosis and Thrombosis</i> , Vol. 14, No. 10, 1529-1533 (Oct. 1994).				
GJL	G31	VERMA, et al., <i>Nature</i> , Vol. 389, pp. 239-242 (1997).				
GJL	G32	SHEARS, et al., <i>J. Am. Coll. Surg.</i> , Vol. 187, pp. 295-306 (1998).				
GJL	G33	SAWA, et al., <i>Circulation</i> , Vol. 96 (Suppl. II) 280-285 (1997).				

Examiner Signature	Jeffrey E. Russel	Date Considered	September 7, 2004
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: July 16, 2004

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Sheet 3 of 3

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<b>Group Art Unit</b>	1654
<b>Examiner Name</b>	J. Russel

Attorney Docket Number 080618-0237

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
RJL	G34	BAI, et al. <i>Ann. Thorac. Surg.</i> , Vol. 66, pp. 814-820 (1998).	
RJL	G35	LUI, et al., <i>Current Pharmaceutical Design</i> , Vol. 2, pp. 553-584 (1996).	
RJL	G36	MARSHALL, et al., <i>Science</i> , Vol. 269, pp. 1050-1055 (Aug. 1995).	
RJL	G37	ORKIN, et al. "Report and Recommendations of the Panel to Assess the NIH Investment on Research in Gene Therapy", (1995).	
RJL	G38	ROČIĆ ET AL., "L-arginyl-L-lysine and L-arginyl-L-arginine", <i>Med. Sci. Res.</i> (1990), Vol. 18, pp. 165-166.	
RJL	G39	ADAMS ET AL., "Oral L-Arginine Inhibits Platelet Aggregation but Does Not Enhance Endothelium-Dependent Dilation in Healthy Young Men", <i>JACC</i> (October 1995), Vol. 26, No. 4, pp. 1054-1061.	
RJL	G40	MAYER ET AL., "Homocysteine and Coronary Atherosclerosis," <i>JACC</i> (March 1, 1996), Vol. 27, No. 3, pp. 517-527.	
RJL	G41	Supplementary European Search Report dated May 12, 2004 for EP Application No. 97938163.9	
RJL	G42	International Search Report dated August 29, 1994 for PCT Application No. PCT/US94/06203.	
RJL	G43	International Search Report dated January 21, 1997 for PCT Application No. PCT/US96/17241.	
RJL	G44	International Search Report dated October 10, 1997 for PCT Application No. PCT/US97/13905.	

Examiner Signature

Jeffrey E. Russel

Date Considered

September 7, 2004

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